

CLAIMS

We claim:

1. An isolated nucleic acid molecule encoding a caspase-14 polypeptide or functional fragment thereof.
2. The isolated nucleic acid molecule of claim 1, comprising a contiguous single stranded or double stranded nucleotide sequence of SEQ ID NO:4.
3. The isolated nucleic acid molecule of claim 2, wherein said single stranded nucleotide sequence comprises a contiguous nucleotide sequence of coding strand or non-coding strand.
4. The isolated nucleic acid molecule of claim 1, which encodes the amino acid sequence of SEQ ID NO:5 or a splice variant thereof.
5. An isolated nucleic acid molecule, comprising at least 12 contiguous nucleotides of the nucleic acid molecule of claim 1 or SEQ ID NO:4, provided that said contiguous nucleotides do not consist entirely of positions 430 to 450 of SEQ ID NO:4, positions 436 to 453 of SEQ ID NO:1, the expressed sequence tag having GenBank accession number AA103647, or any contiguous portion thereof.
6. An isolated nucleic acid molecule, comprising a caspase-14 gene or functional fragment thereof.
7. The isolated nucleic acid molecule of claim 6, wherein said functional fragment is a regulatory element.
8. A vector, comprising the nucleic acid molecule of claim 1.

9. The vector of claim 8, which is a viral vector.
10. An expression vector, comprising the nucleic acid molecule of any one of claims 1-7, wherein the nucleic acid molecule is operatively linked to a promoter.
11. A host cell containing the vector of claim 8.
12. An isolated caspase-14 polypeptide or functional fragment thereof.
13. The isolated polypeptide of claim 12, comprising SEQ ID NO:5 or a splice variant thereof.
14. The polypeptide of claim 12, comprising a functional fragment of SEQ ID NO:5 or a splice variant thereof.
15. The polypeptide of claim 12, wherein said functional fragment comprises a large subunit of caspase-14.
16. The polypeptide of claim 12, wherein said functional fragment comprises a small subunit of caspase-14.
17. The polypeptide of claim 14, wherein said functional fragment comprises contiguous amino acid sequences selected from the group consisting of positions 1 to 146 of SEQ ID NO:5, positions 1-146 of SEQ ID NO:7, and positions 1-118 of SEQ ID NO:9.
18. The polypeptide of claim 14, wherein said functional fragment comprises contiguous amino acid sequences selected from the group consisting of positions 147 to 242 of SEQ ID NO:5, positions 147-230 of SEQ ID NO:7, and positions 119-214 of SEQ ID NO:9.

19. The polypeptide of claim 15, wherein said large subunit is fused to a small subunit of a polypeptide selected from the group consisting of caspase-1, caspase-2, caspase-3, caspase-4, caspase-5, caspase-6, caspase-7, caspase-8, caspase-9, caspase-10 and ced-3.

20. The polypeptide of claim 16, wherein said small subunit is fused to a large subunit of a polypeptide selected from the group consisting of caspase-1, caspase-2, caspase-3, caspase-4, caspase-5, caspase-6, caspase-7, caspase-8, caspase-9, caspase-10 and ced-3.

21. An anti-caspase-14 antibody.

22. The antibody of claim 21, which is a monoclonal antibody.

23. A cell expressing the antibody of claim 22.

24. An anti-idiotypic anti-caspase-14 antibody.

25. A method for identifying a compound that modulates caspase-14 activity, comprising the steps of:

a) contacting a sample containing a caspase-14 polypeptide or functional fragment thereof with a test compound; and

b) determining the activity of said caspase-14 polypeptide or functional fragment thereof, wherein a change in activity indicates a compound that modulates caspase-14 activity.

26. The method of claim 25, wherein said compound inhibits caspase-14 activity.

27. The method of claim 25, wherein said compound enhances caspase-14 activity.
28. The method of claim 25, wherein said caspase-14 activity is apoptotic activity.
29. The method of claim 25, wherein said caspase-14 activity is determined by a binding assay.
30. The method of claim 25, wherein said caspase-14 activity is enzymatic activity.
31. The method of claim 30, wherein said enzymatic activity is determined by contacting said caspase-14 polypeptide or functional fragment thereof with a fluorescent substrate.
32. The method of claim 31, wherein said fluorescent substrate is selected from the group consisting of DEVD-AMC and YVAD-AMC.
33. The method of claim 25, wherein said sample comprises a cell lysate.
34. The method of claim 25, wherein said sample comprises an isolated caspase-14 polypeptide or functional fragment thereof.
35. The method of claim 25, wherein said compound is a small molecule.
36. The method of claim 25, wherein said compound is an anti-caspase-14 antibody.

37. The method of claim 25, wherein said compound is an anti-idiotypic anti-caspase-14 antibody.

38. A method of identifying inhibitors or enhancers of caspase-14 activity comprising:

a) contacting an activated caspase-14 with a substrate in the presence of a test compound under conditions in which the caspase-14 processes the substrate in the absence of the test compound; and thereafter

b) detecting increased or decreased substrate turnover, wherein increased substrate turnover indicates the presence of an enhancer and wherein decreased substrate turnover indicates the presence of an inhibitor.

39. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO:6.

40. The isolated nucleic acid molecule of claim 1, comprising the nucleotide sequence of SEQ ID NO:8.

41. The isolated polypeptide of claim 12, comprising the polypeptide sequence of SEQ ID NO:7.

42. The isolated polypeptide of claim 12, comprising the polypeptide sequence of SEQ ID NO:9.

43. An isolated nucleic acid molecule encoding a human caspase-14 polypeptide.

44. An isolated human caspase-14 polypeptide.

45. The isolated nucleic acid molecule of claim 1, which comprises a contiguous single stranded or double stranded nucleotide sequence of SEQ ID NO:1.

46. The isolated nucleic acid molecule of claim 2, wherein said single stranded nucleotide sequence comprises a contiguous nucleotide sequence of coding strand or non-coding strand.

47. The isolated nucleic acid molecule of claim 1, which encodes the amino acid sequence of SEQ ID NO:2.

48. An isolated nucleic acid molecule, comprising at least 12 contiguous nucleotides of the nucleic acid molecule of claim 1 or SEQ ID NO:1, provided that said contiguous nucleotides do not consist of positions 454 to 474 of SEQ ID NO:1, positions 460 to 477 of SEQ ID NO:1, the expressed sequence tag having GenBank accession number AA103647, or any contiguous portion thereof.

49. An isolated nucleic acid molecule, comprising a caspase-14 gene or functional fragment thereof.

50. The isolated nucleic acid molecule of claim 6, wherein said functional fragment is a regulatory element.

51. An expression vector, comprising the nucleic acid molecule of any one of claims 45-50, wherein the nucleic acid molecule is operatively linked to a promoter.

52. The isolated polypeptide of claim 12, comprising SEQ ID NO:2.

53. The polypeptide of claim 12, comprising a functional fragment of SEQ ID NO:2.

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55. The polypeptide of claim 53, wherein said functional fragment comprises positions 163 to 257 of SEQ ID NO:2.